Modeling Cyclic Variation of Intracranial Pressure

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Abstract: To test the theoretical feasibility that low frequency baseline changes of the intracranial pressure (ICP) recording during mechanical ventilation are due to cyclic extravascular compressional modulation primarily of the cerebral venous bed, an established isovolumetric model of cerebrospinal fluid dynamics proposed by Ursino was modified [1,2]. These modifications were made to address the hypothesis that: 1) cyclic extravascular compressional modulation of the cerebral venous bed occurs during positive pressure inhalation; and 2) the degree of modulation is diminished with increasing vascular dilation induced by increasing the level of the partial pressure of carbon dioxide (PCO_2) within the arterial blood. Modification of the isovolumetric model was accomplished by introducing a cyclic modulation of the resistance of the cerebral venous bed synchronized with ventilation. Simulated model recordings demonstrated that the correlation index between arterial blood pressure and ICP progressively increased monotonically as the level of PCO_2 increased from 30 mmHg to 80 mmHg. These results support the premise that during positive pressure ventilation, cyclic extravascular compressional modulation of primarily the cerebral venous bed produces a cyclic variation of ICP and the degree of modulation is dependent on the state of vascular dilation.

Key Words: intracranial pressure, mathematical model

I. INTRODUCTION

Laboratory findings have demonstrated that the dynamic features of the intracranial pressure (ICP) recording are known to change depending on the state of cerebral vascular dilation. About two decades ago Portnoy and his colleagues demonstrated from laboratory studies on normocapnic preparations that during normal tone the arterial and intracranial pressure signals do not look similar [3,4]. As shown in Fig. 1a, during normal vascular tone, unlike the arterial blood pressure (ABP) recording, the ICP

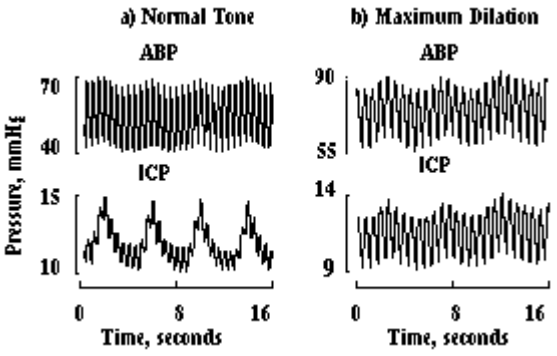

Figure 1. Experimental Recordings of ABP and ICP during Normocapnia and Hypercapnia. a) Normocapnia with Intact Tone. ABP and ICP recordings are not similar. b) Hypercapnia with Maximum Dilation. ABP and ICP recordings are markedly similar.

recording demonstrates a cyclic low-frequency variation in the baseline corresponding to the ventilation. As a result, the ICP recording is not similar to the ABP recording. In contrast, during deep hypercapnia and maximal vascular dilation, the ABP and ICP recordings look very similar (see Fig. 1b) [3,4]. The numerical approach this earlier group used to characterize their laboratory findings was to examine changes in the coherence function derived from the ICP and ABP recordings. When the ICP and ABP recordings are nearly identical the coherence function approaches unity. Generally, their observations and the observations of others using a systems approach have suggested that the more similar the spectral components of the ICP recording are to those of the ABP recording, the more likely cerebral autoregulation is impaired [3,5,6].

More recently, our group has reproduced the earlier experimental findings of Portnoy and his colleagues [7,8]. However, we have developed a different numerical approach. Since correlation analysis of two signals in the time domain is analytically equivalent to coherence analysis in the frequency domain, we used correlation analysis [7,8]. In particular, as the ICP and ABP recordings become more similar, the maximum value of the correlation function approaches unity, which indicates loss of vascular tone [7,8]. Our clinical findings from brain injured pediatric trauma cases indicate that a high correlation (r-value > 0.85) between the ABP and ICP recordings is often demonstrated in pediatric brain trauma patients [9].

In order to make the consistent laboratory findings described above more clinically useful, an understanding of the mechanism(s) which underlies the changes of ICP recordings with increasing cerebral dilation must be determined. The cyclic variation of intrathoracic pressure during positive pressure ventilation is considered a major causal factor of the corresponding synchronized variation of ICP [10]. From laboratory preparations with cranial window placement we have observed that the brain also undergoes cyclic movement synchronized with ventilation and occasionally noted an apparent blanching of some pial veins at their emergence sites from the brain parenchyma during the positive pressure inhalation phase. Furthermore, we have reported that flow through the pial veins is uniformly lower during positive pressure inhalation for all states of cerebral vascular dilation [8]. From these observations, we suspect that the mechanism(s) that controls the dynamic characteristics of the ICP recording over the ventilation cycle are up-stream from the pial veins at vascular sites within the parenchyma. As a result, we have developed a premise that: 1) cyclic extravascular compression primarily of the cerebral venous

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Abstract

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bed occurs during positive pressure inhalation; and 2) the degree of extravascular compression is diminished with increasing vascular dilation.

Mathematical models of various aspects of the dynamics of cerebrospinal fluid and intracranial pressure include descriptions of the compressional influence of ICP on the cerebral vasculature. In particular, Starling resistors have been used to describe the consequences of the collapsibility of bridging veins and the capillary and venous bed on ICP dynamics and cerebral blood flow [11,12]. However, because of its quantitative capability to simulate the dynamics of an ICP recording the model of CSF dynamics proposed by Ursino was the only model suitable to test the theoretical feasibility that extravascular compressional modulation is a causal factor underlying the synchronized cyclic variation of ICP with positive pressure ventilation [1,2]. Ursino's isovolumetric model of CSF dynamics is an analogue electrical circuit that is based on the Monro-Kellie doctrine [1,2]. This doctrine requires that the overall volume of the craniospinal sac remains constant. Moreover, because this sac contains three volume compartments, cerebrospinal fluid, blood, and brain tissue, any increase or decrease of volume in one compartment must be compensated for by corresponding net decrease or increase in the other compartments [1,2].

The goal of this study was to test the feasibility of our hypothesis for the mechanism(s) that causes the cyclic variation of the ICP waveform by modifying the isovolumetric model of CSF dynamics proposed by Ursino [1,2]. Specifically, by evaluating a comparison between reported laboratory results and model simulations we theoretically address the hypothesis that: 1) cyclic extravascular compression primarily of the cerebral venous bed occurs with positive inhalation; and 2) the degree of extravascular compression is diminished with increasing vascular dilation induced by increasing PCO_2

II. METHODS

The protocol for this study was reviewed and approved by the IRB committees of both universities involved. Four pigs ranging in weight from 1.8 to 3.3 kg were used in this study. The procedures used were similar to those described for other animal studies employing this cranial window preparation [7,8]. ICP and ABP recordings were obtained digitized at a rate of 250 Hz with a system previously described [7,8].

The quantitative model of intracranial hydrodynamics proposed by Ursino [1,2] is the electric circuit analogue model shown in Figure 2. This model is based on the Monroe Kellie doctrine that requires that the overall volume within the craniospinal sac remains constant. The principal volume components contained within the sac are tissue, blood, and cerebrospinal fluid. For the normal tone conditions, resistance values of R_{a1}, R_{a2}, R_{a3}, R_{pv}, R_f, R_{ve}, and R_{vo} are 1.19, 1.19, 2.38, 3.21, 2387, 0.17, and 527 mmHg sec cm^{-1} respectively. Also, the capacitance values for this condition of C_{a1}, C_{a2}, C_{ve}, C_{ic}, and C_{vi} are .0.006, 0.003, 2.34, 0.2, and 0.46 $cm^3 mmHg^{-1}$ respectively.

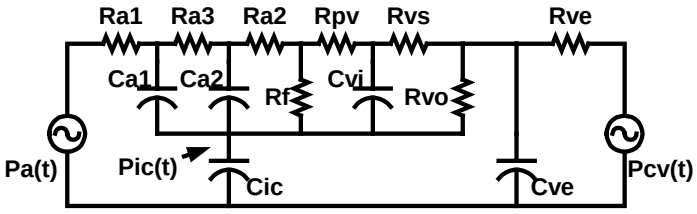

Figure 2. Analogue Electric Circuit Model of Mathematical Description of Cerebrospinal Fluid Dynamics. Inputs to this model were experimental recordings of arterial and jugular blood pressure. State equations were developed by nodal analysis.

To simulate cyclic extravascular compression of the vasculature, the primary modification was to implement a synchronized cyclic modulation of the resistance of small arterioles, capillary bed and small venules at the frequency of mechanical ventilation. During the positive-pressure phase of inhalation the resistance progressively increases and during passive exhalation the resistance decreases back to a steady state baseline value. Formulations of steady-state values of resistance at each level of hypercapnia were based on lab measurement of the diameters of pial arterioles and venules where arteriolar diameter increased from 52 to 72 um and venule diameter increased from 41 to 44 um [8]. Excluding R_{pv}, R_f, and R_{vo}, for each increased level of PCO_2 from 30 to 80 mmHg resistance decreased by approximately 25%. With an initial value of cerebral venous resistance, R_{vs}, of 1.24 mmHg sec cm^{-1}, the temporal scheme of modulation employed was as follows: a) during inhalation cerebral venous resistance, R_{vs}, increased as 1-exp(.004 t) and during expiration decreased as exp(.004t). This cyclic modulation of R_{vs} was systematically reduced with increasing level of simulated PCO_2. Laboratory recordings of arterial pressure, $P_a(t)$, and venous jugular pressure, $P_{cv}(t)$, were used as inputs to the model. Using nodal analysis and defining the intravascular pressures in large and small arteries, cerebral arterial pressure, and intracranial pressures as the states of the circuit, the resultant state equations were implemented by the use of MATLAB and SIMULINK software (Mathworks, Inc., Natick, MA).

III. RESULTS

Comparisons of experimental and simulated recordings of ICP produced by the modified model during conditions of normocapnia and hypercapnia are shown in Figure 3. For the condition of normocapnia and intact vascular tone, both the experimental and simulated ICP recordings increase during the positive pressure phase of ventilation and abruptly decrease back to a steady-state baseline value during passive expiration (see Fig 3a and 3b). The experimental recording was obtained at a PCO_2 level of 35 mmHg (see Fig. 3a). Simulation of the corresponding ICP recording was obtained by using the resistance values given above (see Fig. 3b). In contrast, during a deep hypercapnic condition, the experimental ICP recording obtained at an arterial blood level of PCO_2 of 78 mmHg does not exhibit a salient increase during the inhalation phase of ventilation (see Fig. 3c).

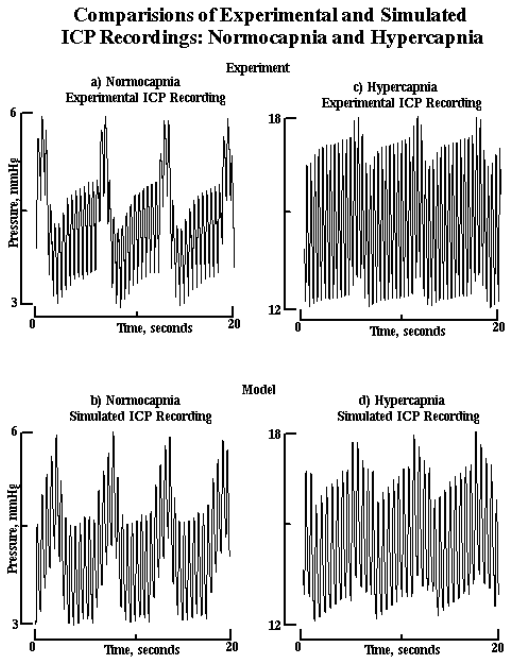

Figure 3. Comparison of Experimental and Simulated ICP for Conditions of Normocapnia and Hypercapnia. a) Experimental ICP Recording during Normocapnia and Intact Vascular Tone. b) Simulated ICP Recording for Condition of Normocapnia with Intact Vascular Tone. The recordings shown in a) and b) are markedly similar. During the positive pressure phase of ventilation, ICP saliently increases. At the onset of passive expiration, there is an abrupt decrease of ICP. Experimental and simulated recordings for the hypercapnic condition shown in c) and d) are markedly similar.

The simulated hypercapnic ICP recording was obtained using the minimal modulation value at a PCO_2 level of 80 mmHg (see Fig. 3d). Using a previously described correlation index [8] the numerical similarity between the ABP and ICP recordings for each simulated level of PCO_2 was computed. For the normocapnic condition, both the experimental and simulated correlation indices were equivalent with the value of 0.69. For the deep hypercapnic condition the correlation indices for the experimental and simulated recording were 0.92 and 0.96 respectively. Using the described modulation scheme of cerebral venous resistance, the correlation index computed from the corresponding simulated ICP responses was determined for each simulated level of PCO_2. As the strength of modulation of the venous bed was reduced, the correlation index monotonically increased from a minimum value of .69 at a PCO_2 level of 30 mmHg to maximum value of .96 at a level of 80 mmHg (see Fig. 4).

IV. DISCUSSION

To test the feasibility of the hypothesis that localized sites within the cerebral venous bed undergo extravascular compressional modulation during positive pressure ventilation, Ursino's electric circuit model of cerebral hemodynamics was modified. In particular, during normocapnia and intact vascular tone, the baseline of ICP demonstrates a low frequency variation

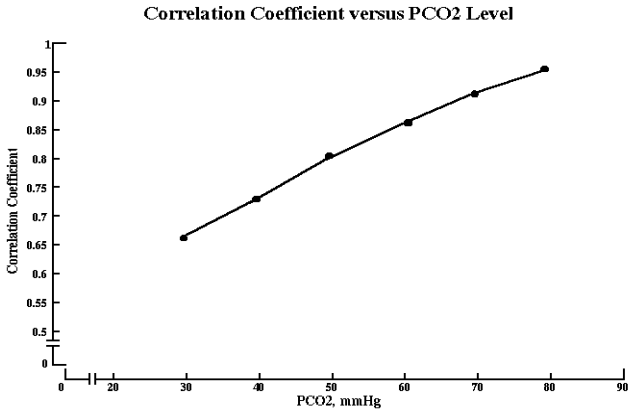

Figure 4. Computed Correlation Index from Simulated ABP and ICP Recordings versus Simulated Level of PCO_2. Using a previously described correlation index to assess the similarity between the ABP and ICP recordings at each level of PCO_2, the value of the index for the simulated recordings was determined to increase monotonically with increasing level of PCO_2.

with a distinct phasic increase synchronized with the onset of positive pressure inhalation and a rapid decrease at the onset of the passive expiration phase of ventilation (see Fig. 1). In contrast, during maximum dilation induced by deep hypercapnia, the low frequency variation of the baseline of ICP is nearly absent. In Fig. 3, comparisons of experimental and simulated ICP recordings for the conditions of normocapnia with intact tone and deep hypercapnia with maximal dilation are shown. These two conditions were simulated by maximal modulation of the resistance of the venous bed during normocapnia and minimal modulation during deep hypercapnia. Because of the distinct low frequency variations of the baseline of the ICP during normal tone, the ICP recording is dissimilar to the ABP recording (see Fig 1a). In contrast during deep hypercapnia, the distinct low frequency variation in the baseline of the ICP recording is not as evident (see Fig 1b). As a result, the ICP and ABP recordings are similar and correlate strongly. By progressively reducing the strength of modulation of the resistance of the cerebral venous bed, the correlation between the ICP and ABP monotonically increased from a minimum value of .69 at maximum modulation to a maximum value of .96 at minimum modulation (see Fig. 4).

Because of experimental findings that the bridging veins into the lateral lacunae become compressed with increased ICP [13], most models which describe cerebral blood flow and ICP dynamics include at least one Starling resistor within the venous vasculature[1,2,11,12,14]. However, numerous veins by-pass the lateral lacunae and connect directly to the sagittal sinus [15], and it has been reported that at least some of these bridging veins do not collapse during intracranial hypertension [16]. Moreover, because of our reported observations that flow through the pial veins is uniformly lower during positive pressure inhalation for all states of cerebral vascular dilation [8], we suspect that changes of venous resistance within the brain parenchyma at numerous sites within the mesh of the drainage network not related to connections to either the lateral lacuna or sagittal sinus probably occur. At these sites the extravascular pressure

approaches or exceeds the transmural venous pressure. For simplicity we chose to define an equivalent Starling resistor for all the possible major sites of venous compression.

The results of this study demonstrate that by modulating the cerebral venous resistance, it is possible to generate ICP recordings that match experimental recordings obtained over a range of vascular states. Specifically, by systematically decreasing the amplitude of modulation with increasing level of simulated arterial PCO_2 and vascular dilation, the correlation of the ABP and ICP recordings monotonically increases as reported [8]. The linkage between cyclic variation of intrathoracic pressure during positive pressure ventilation which is considered a primary causal factor in the synchronized variation of ICP [10] with ventilation, is probably related to two separate mechanisms: 1) variation of sagittal pressure and 2) compression of the boundaries of the craniospinal sac. Cyclic compression of the venous vasculature within the thoracic produces a corresponding cyclic variation of sagittal sinus pressure with positive pressure ventilation. Increased sagittal sinus pressure generates an increase of cerebral venous blood volume that produces an increase of ICP and a decrease of cerebral perfusion pressure. Thus, extravascular pressure is increased, and transmural pressure within the venous network is lowered. Also as noted earlier, a cyclic movement of the brain occurs during the positive pressure ventilation. It seems likely this movement that is observed even after death of the laboratory preparation is produced from cyclic compression of the craniospinal sac produced by transmission of the thoracic pressure through body tissue and interstitual fluid. Thus, during compression of the craniospinal sac, ICP will increase which in turn would produce additional compression at critical venous sites vulnerable to the Starling phenomenon. Thus, cyclic compression of the craniospinal sac would work in synergy with cyclic changes of sagittal sinus pressure to produce a modulation of the venous resistance over the ventilation-cycle.

In summary, simulated ICP recordings that are similar to experimental ICP recordings are obtained by modulation of the venous resistance pathway in the isovolumetric model of cerebral spinal fluid proposed by Ursino [1,2]. Furthermore, by systematically diminishing the strength of modulation with increasing vascular dilation, the modified model predicts the increasing strength of correlation between the ABP and ICP recordings with increasing depth of hypercapnia and vascular dilation. The potential clinical application of these results is that patients with severe head-injury who demonstrate a strong correlation between the ICP and ABP pressure recordings are likely to have a high transmural venous pressure indicative of maximal dilation, loss of autoregulation of cerebral blood flow, and the subsequent development of cerebral edema.

V. CONCLUSION

The feasibility that changes of the dynamic features of the ICP recording linked to positive pressure ventilation can be simulated by a modification of the isovolumetric model proposed by Ursino [1,2] has been demonstrated. The modification is accomplished by introducing a cyclic modulation of the resistance of the cerebral venous bed synchronized with ventilation. The degree of modulation is diminished with increasing state of vascular dilation.

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